REMARKS

This amendment is responsive to the Office Action mailed May 4, 2007. Reconsideration and allowance of claims 1-20 are requested.

The Office Action

Claims 1-17 stand rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Maier et al., U.S. Publ. Appl. 2001/0039377 (hereinafter "Maier").

The Office Action additionally cited certain informalities in the claims, which are addressed by amendments herein.

The Maier reference

The Maier reference relates to diffusion tensor imaging. The apparent diffusion coefficient (¶[0007]) is measured based on the equation $S=S_0\exp(-bD)$ (¶[0012]) where b is the "b-factor" or sensitivity factor, D is the apparent diffusion coefficient, and S_0 is the signal level at b=0. Thus, one measures the signal at several values of the b-factor and plots the natural logarithm of S vs. b to obtain D. (¶[0014]). This is shown in Maier Fig. 1 for *ex vivo* neat solutions of water, ethanol, and isopropanol. However, the apparent diffusion coefficient D is actually a tensor, i.e., it varies depending upon the direction along which the diffusion coefficient is measured, and so one generally wants to repeat this process along three or, more preferably, six directions in order to obtain the components of the D tensor. (¶[0019]).

However, there is a problem in extending this to *in vivo* settings -- these measurements take a substantial period of time. As noted in the present application, for example, a typical time for a single measurement at a single b-factor value is about 1-3 seconds, which severely constrains the number of samples that can be acquired if, for example, the patient is expected to hold his or her breath during the procedure. (Present application at page 6 lines 31-33).

Accordingly, Maier teaches acquiring one sample at a low b-factor and another sample at a high b-factor (e.g., b=1000 s/mm^2) and making a two-point slope estimate of the diffusion coefficient D for each direction. (Maier ¶[0019]). Based on ¶[0019] it appears that only the high b-factor value is repeated -- the low b-factor value seems to be a single acquisition at b=0. Applicants find no suggestion in Maier

of performing the low b-factor measurement in different directions, and the Office Action does not appear to suggest otherwise.

Maier, like the present application, recognizes that at low b-factor the signal has a substantial perfusion component. (Maier ¶[0021], present application at page 2 lines 24-25). Thus, while the high b-factor (e.g., b=1000 s/mm^2) measurement conforms with the equation $S=S_0\exp(-bD)$, the low b-factor measurement does not conform with this equation, and so the estimated value for S_0 that was expected to be derived from the low b-factor measurement is wrong, due to perfusion effects.

Maier explains: "Diffusion coefficients determined by signal sampling at different b-factors between 0 and 1000 sec/mm^2, therefore, are currently usually referred to as 'apparent diffusion coefficients' (ADC), rather than more generically as diffusion coefficients D." (¶[0021]). However, this does not concern Maier overmuch, as shortly thereafter it is stated: "the overall effect [of perfusion] is deemed to be negligible, due to the small blood volume fraction and to be limited to the b-factors under the 300 sec/mm^2 range." (¶[0023]).

To summarize, Maier teaches determining a diffusion tensor (not a perfusion tensor) by acquiring a data point at low b-factor (e.g., b=0) and a plurality of data points at high b-factor (e.g., b=1000) in different directions, and estimating the apparent diffusion coefficient in each direction by a two-point slope estimate. Maier recognizes that the low b-factor measurement may have a small error due to perfusion, but concludes that any such error has negligible effect on the computed diffusion tensor.

The present application

The present application goes far beyond Maier. The present application recognizes that at low b-factor the signal is mostly due to perfusion and not diffusion effects. (Present application at page 2 lines 24-25). However, where Maier saw this as having a negligible effect on the diffusion tensor measurement, the inventor of the present application had the insight that this could provide an opportunity to develop a completely new diagnostic tool for determining the perfusion tensor.

The inventor recognized that the expression $S/S_0=\exp(-bD)$ of Maier is more accurately $S/S_0=f\cdot\exp(-bP)+(1-f)\cdot\exp(-bD)$ (Present application Equation (2))

with perfusion signal component f·exp(-bP) decaying much more rapidly than diffusion signal component (1-f)·exp(-bD) at low sensitivities. (Present application at page 4 lines 25-28). Based on this further insight, the present application discloses that by acquiring measurements in different directions at low sensitivity e.g., b<50 s/mm^2, for example, and preferably between 5 s/mm^2 and 15 s/mm^2, (page 2 lines 20-21) and obtaining slopes or other derivative information from these low sensitivity acquisitions and an acquisition at still lower sensitivity (e.g., at b~0 s/mm^2) one could obtain a reasonable estimate of the perfusion tensor.

In another embodiment, the inventor recognized that, although the foregoing provides a reasonable estimate of the perfusion tensor, it may have some error due to the contribution of the diffusion signal component (1-f)·exp(-bD) which, although slower decaying at low sensitivity values, may have some impact on the slope. Accordingly, in some disclosed embodiments additional acquisitions are made at higher sensitivities, e.g. b=200 s/mm^2 and b=800 s/mm^2, and the slope derived from those measurements (where the diffusion signal component dominates over the perfusion signal component) is used to determine the diffusion tensor D. In this case, one can apply the full expression $S/S_0=f\cdot\exp(-bP)+(1-f)\cdot\exp(-bD)$ with the diffusions signal component (1-f)·exp(-bD) known (since D is now known) to more precisely determine the perfusion tensor. These embodiments are described at least at page 5 line 26-page 25.

In a variation described starting at page 6 line 26, the lower high sensitivity measurements are omitted (e.g., the 200 s/mm^2 data points), and one or more of the low sensitivity measurements used for the perfusion tensor determination is also used as the lower data point for the diffusion tensor determination.

The Claims Distinguish Patentably Over the References of Record

Claim 1 calls for a method of perfusion imaging comprising: performing a first magnetic resonance data acquisition with gradient encodings for random motion at a first sensitivity value; performing a set of at least six second magnetic resonance data acquisitions with gradient encodings for random motion in different directions at second sensitivity values larger than the first sensitivity value; and determining a perfusion tensor based on the magnetic resonance data acquisitions.

As noted in the Office Action, Maier discloses a first magnetic resonance data acquisition with gradient encodings for random motion at a first sensitivity value (the low b-factor acquisition of Maier) and further discloses performing a set of at least six second magnetic resonance data acquisitions with gradient encodings for random motion in different directions at second sensitivity values larger than the first sensitivity value (the high b-factor acquisitions at about b=1000 s/mm^2).

However, Applicants respectfully submit that Maier does not disclose or fairly suggest determining a perfusion tensor based on the magnetic resonance data acquisitions. At most, Maier recognizes that the low b-factor acquisition may have a small error due to perfusion, which Maier concludes is negligible. Merely performing an acquisition that is influenced by perfusion does not disclose or fairly suggest determining a diffusion tensor from the acquisition.

Moreover, one cannot in fact determine the perfusion tensor from the acquisitions performed by Maier. These acquisitions provide (for each direction) one datum at low b-factor and another datum at high b-factor (e.g., 1000 s/mm^2). From this data, Maier correctly concludes that one can extract the diffusion tensor, possibly with some small (negligible) error due to influence of perfusion. One cannot extract the perfusion tensor from this data, because the high b-factor datum has virtually no influence from the fast-decaying perfusion signal component.

The Office Action also appears to argue, based on reference to a general purpose dictionary, that diffusion and perfusion are synonymous. This argument is contradicted by both the disclosure of the present application and by the cited Maier reference, both of which clearly and unambiguously treat perfusion and diffusion as distinct and different terms of art.

Extrinsic evidence, such as dictionaries, are generally less reliable than the specification in determining how to read claims. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1318 (Fed. Cir. 2005). A dictionary by definition is not part of the specification and does not have the specification's virtue of being created for the purpose of explaining the patent's scope and meaning, and is unlikely to result in a reliable interpretation of claim scope unless considered in the context of the specification. *Id.* at 1318, 1319. General-purpose dictionaries are especially problematic as they are not art-related, and a general-purpose dictionary definition cannot be used to overcome

art-specific evidence as to the meaning of a claim term. *Id.* at 1321, 1322. Although dictionaries may be consulted, a dictionary definition cannot be used to contradict a definition found in or ascertained by reading the specification. *Id.* at 1322-23.

Respectfully, the Office Action's suggestion, based on a general-purpose dictionary definition, that perfusion and diffusion are synonymous is directly contradicted both by the specification of the present application and by art-specific evidence including at least the very reference (Maier) applied by the Office Action.

Claim 2 further calls for the second sensitivity values being below 50 s/mm^2. Nowhere does Maier disclose or fairly suggest that the high sensitivity measurements, which the Office Action equates with the measurements at the second sensitivity values, be acquired at sensitivity values being below 50 s/mm^2. The 0-1000 s/mm^2 range specified in Maier ¶[0021] encompasses both the low b-factor and the high b-factor acquisitions. Maier expressly calls for the high b-factor acquisitions to be at sensitivities typically on the order of 1000 s/mm^2 (¶[0019]). Still further, Maier expressly warns that acquisitions at sensitivities under 300 s/mm^2 are likely to have substantial undesired perfusion effects, which strongly teaches away from acquiring the high b-factor acquisitions at below 50 s/mm^2.

Claim 3 calls for the first sensitivity value to be substantially zero and for the second sensitivity values being between five and thirty. The comments on claim 2 pertain also to claim 3.

Claim 5 calls for performing a perfusion tensor visualization. This claim is rejected based on the diffusion tensor trace images disclosed at Maier ¶[0018]. Respectfully, a diffusion tensor trace image is not a perfusion tensor visualization.

Claim 11 has been placed into independent form, and relates to certain embodiments in which the determining of the perfusion tensor includes adjustment for the (small) effect of diffusion at low sensitivity values. One of the second magnetic resonance data acquisitions having the strongest measured signal decay is selected, a third magnetic resonance data acquisition is performed at a third sensitivity value higher than the second sensitivity values, a diffusion coefficient and a fraction value are determined based on the selected second and third magnetic resonance data acquisitions to provide a diffusion signal component, and the diffusion signal component is eliminated from the magnetic resonance data acquisitions to provide a

perfusion signal component, the perfusion tensor being determined from the perfusion signal components.

At most Maier discloses determining a diffusion tensor. Maier does not contemplate additionally determining a perfusion tensor, much less doing so using the method set forth in claim 11.

Claim 12 calls for computer program product comprising a digital storage medium storing a perfusion imaging program executable to perform a method including determining a perfusion tensor based on a first magnetic resonance data acquisition and a set of at least six second magnetic resonance data acquisitions, the first magnetic resonance data acquisition being performed at a first sensitivity value and the second magnetic data resonance data acquisitions being performed at a second sensitivity value with gradient encodings in different directions, the first sensitivity value being below the second sensitivity values, and further executable to perform perfusion tensor imaging.

Maier does not disclose a computer program product comprising a digital storage medium storing a perfusion imaging program executable to perform a method including determining a perfusion tensor. To the contrary, even though Maier recognizes that the low sensitivity measurements may be influenced by perfusion, Maier does not recognize that such influence might enable one to determine the perfusion tensor. Moreover, Maier does not disclose or fairly suggest a computer program product comprising a digital storage medium storing a perfusion imaging program executable to perform a method including performing perfusion tensor imaging. To the contrary, Maier considers any influence of perfusion at low sensitivities to be merely a source of error in Maier's diffusion tensor measurements, and indeed considers such perfusion influence to be a negligible error at that.

Claim 17 calls for perfusion imaging apparatus comprising a magnetic resonance data acquisition device, and a computer system programmed to cause the magnetic resonance data acquisition device to perform a first magnetic resonance data acquisition at a first sensitivity value and to perform a set of at least six second magnetic resonance data acquisitions with gradient encodings in different directions at second sensitivity values below 50 s/mm^2, the first sensitivity value being smaller

than the second sensitivity values. The computer system is further programmed to determine a perfusion tensor based on the magnetic resonance data acquisitions.

Maier does not disclose or fairly suggest a computer system programmed to cause a magnetic resonance data acquisition device to perform a first magnetic resonance data acquisition at a first sensitivity value and to perform a set of at least six second magnetic resonance data acquisitions with gradient encodings in different directions at second sensitivity values below 50 s/mm^2, the first sensitivity value being smaller than the second sensitivity values. Indeed, to do so would defeat the purpose of Maier, which is to determine a diffusion tensor, because Maier teaches that such acquisitions would suffer from interference due to perfusion. Rather, Maier teaches performing one of the acquisitions at high b-factor, e.g. of order b=1000 s/mm^2, so as to provide diffusion content free of interference from perfusion.

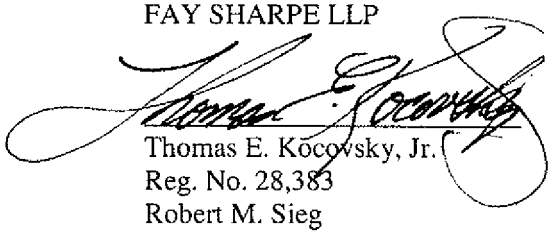
CONCLUSION

For the reasons set forth above, it is submitted that claims 1-20 distinguish patentably over the references of record and meet all statutory requirements. An early allowance of all claims is requested.

In the event personal contact is deemed advantageous to the disposition of this case, the Examiner is requested to telephone the undersigned at (216) 861-5582.

Respectfully submitted,

FAY SHARPE LLP



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